



I do not want my house to be walled in on all sides and my windows to be stuffed. I want the cultures of all the lands to be blown about my house as freely as possible. But I refuse to be blown off my feet by any.

Mahatma Gandhi

Hazards for Skaters and Swimmers

People often retreat to indoor recreational facilities to escape the allergens and pollen of summer, but new evidence shows that the air in such facilities may pose its own threat to respiratory health. Environmental health experts at the Harvard School of Public Health in Boston, Massachusetts, have found that levels of nitrogen dioxide (NO_2) at indoor skating rinks sometimes exceed air quality guidelines set by the World Health Organization (WHO). Another team of researchers monitoring an indoor water park discovered that bioaerosols caused an outbreak of granulomatous lung disease in lifeguards. Both reports appeared in the December 1998 issue of the *American Journal of Public Health*.

A Harvard team led by environmental health researcher Jonathan Levy conducted air quality testing at 19 ice rinks in the Boston area over three winters. They found that concentrations of NO_2 in the rink air correlated with the type of machine used to clean and resurface the ice. At rinks using propane-powered machines, daily mean NO_2 concentrations averaged 206 parts per billion (ppb)—twice as high as the one-hour level recommended by the WHO. In contrast, gasoline-fueled machines produced 132 ppb NO_2 and electric-powered machines produced 37 ppb.

Numerous earlier reports had documented that exposure to elevated NO_2 causes chest tightness, shortness of breath, and other asthma-like symptoms in skaters, hockey players, coaches, and rink employees. "We picked up where those studies left off," says Levy, adding that they next asked, "Given that there are these health problems, how can we reduce NO_2 levels?"

The best solution the researchers found was to replace propane-fueled machines with electric ones. During the course of the study, four ice rinks made the switch and median NO_2 concentrations fell from 124 ppb to 35 ppb. "If [rinks] can economically buy an electric resurfacer, [they should] by all means do it," recommends Levy. However, the \$72,000 price tag for a basic model may be impractical for smaller rinks. Levy found that engineering controls such as increasing ventilation and tuning resurfacers also reduced NO_2 concentrations by an average of 65%.

In another study of an indoor recreational facility, pulmonologist Cecile Rose



Water hazard. Frequent users of indoor swimming and ice-skating facilities may be at risk for respiratory illnesses due to air contaminants including bacteria and nitrogen dioxide.

and colleagues at the National Jewish Medical and Research Center in Denver, Colorado, traced a high incidence of granulomatous lung disease in lifeguards working at a large aquatic center to exposure to contaminated bioaerosols. Granulomatous lung disease results when immune cells cluster in the lungs and form nodules called granulomas in response to an environmental irritant. "Indoor swimming pools have not previously been identified as sources of granulomatous lung disease," says Rose.

The facility Rose investigated had three pools, two waterfalls, numerous spouts and sprayers, two water slides, and bubbler and mushroom fountains. When the waterfalls and mushroom fountain were turned on, the number of respirable aerosol particles (0.45–0.75 micrometers in diameter) rose 1.4-fold above background levels. Adding a water slide caused a 2.3-fold increase. The number of respirable particles rose 5.2-fold when all water features were in use.

Samples of water collected from sprayer features contained large numbers of gram-negative bacteria, predominantly *Pseudomonas* species. In addition, full use of water features raised mean air endotoxin levels from 3.5- to 8-fold, depending on the location of sampling. The water sprayer's design promoted bacterial growth within its circuits, which were severely corroded. During disuse, bacteria multiplied and then were aerosolized in respirable droplets when the machine was turned on.

Among 23 lifeguards working at the facility, 15 were diagnosed with granulomatous lung disease based on lung biopsies and bronchoalveolar lavage. The majority of the affected lifeguards reported work-related cough, shortness of breath, chest

tightness, and upper respiratory congestion. Those diagnosed with the disease worked more cumulative hours and more hours per week than unaffected lifeguards. The researchers have dubbed the newly recognized condition "lifeguard lung."

Patients with granulomatous lung disease generally improve when removed from exposure to the offending contaminant. Oral steroids may be prescribed to reduce inflammation and help restore lung function. Diagnosis of granulomatous lung disease may be complicated by the fact that its symptoms are the same as other common lung disorders, such as asthma, influenza, and bronchitis.

Granulomatous lung disease could occur in users of any indoor swimming pool with water spray features, warns Rose. The frequency of use of an infected pool elevates the risk. For example, she says, "Swim team members who swim daily would be more likely to get granulomatous lung disease than someone who swims once a month."

The Genetic Connection

Every day, it seems, more diseases and conditions are found to be linked to genetic predisposition. On 10 March 1999, the NIEHS sponsored a symposium entitled "Gene-Environment Interactions in Common Clinical Conditions," where participants discussed the gene-environment link in some of today's most common clinical conditions.

Obesity. According to Rudolph Leibel, a professor of pediatrics and medicine at Columbia University in New York City, the heritability of obesity is as high as 80%. While the environment has been implicated

as an influential factor in most studies of obesity in humans, Leibel says the hormone leptin plays an important role in determining the body's regulation of its fat content.

Among other tasks, leptin communicates to the hypothalamus how much fat is stored in the body and indicates when—as during times of food deprivation—these stores are threatened. (This function was presumably a crucial survival factor in the days before humans had readily and consistently available food supplies.) Mutations in the mouse *Ob* gene and its human counterpart have been found to cause severe deficiencies in the amount of leptin produced. The brain interprets the low leptin level as indicating a dearth of body fat, Leibel says, and the body increases weight in a futile effort to increase the fat-derived signal.

Leptin may also play a role in explaining why obese people often have trouble keeping weight off once they lose it. In a study that was published in the 9 March 1995 issue of the *New England Journal of Medicine*, Leibel and colleagues measured the metabolism of both obese and average-weight subjects while the subjects both maintained their weight and either lost or gained weight. They found that when any of the subjects lost weight, their energy expenditures dropped significantly below the metabolic rate that would have been predicted for the new body weight. This demonstrated that each subject's body, whether average weight or obese, had established for itself a certain amount of fat as being normal and was attempting to regain that established amount.

Genetic variation in the genes that comprise the response cascade for leptin action in the hypothalamus of the brain may, in part, determine what is "normal" body fat for an individual. In research published in the September 1997 issue of *Diabetes* and the March 1999 issue of the *International Journal of Obesity*, Leibel and colleagues at Rockefeller University in New York and the University of Laval in Ontario examined a series of allelic variations in the human leptin receptor and their predicted interrelationships that might be involved in such a "set point"-type mechanism.

Rheumatoid arthritis. Rheumatoid arthritis is a disease of industrialization, occurring only in humans and mainly in modern-day man. This autoimmune disease usually begins in middle age, and one-third of sufferers go on to become fully disabled.

Dennis Carson, director of the Stein Institute for Research on Aging at the University of California at San Diego, theorizes that rheumatoid arthritis arises when the *HLA-B27* gene causes an abnormal immune response to an unknown environmental factor—an immune response that doesn't stop, even after its stimulus is removed. Carson thinks that T cells and B cells produced during the immune response may not be properly cleared from the body and may accumulate in the synovium, a joint membrane that secretes a viscous fluid that lubricates the ligaments, tendons, and bursae. These persistent immune cells may then cause the synovial tissue to granulate, with the granulomas becoming self-perpetuating tissue irritants.

Another theory for explaining rheumatoid arthritis is that by-products of common gut flora such as *Escherichia coli*, *Lactobacillus lactis*, and *Brucella ovis* escape

According to Carson, the antibody cells deposited in the joints may linger for years beyond the initial environmental exposure without causing any trouble. It is only when an infective agent enters the body that the resulting immune response overreacts, triggering a full-blown autoimmune response. Carson believes that a triple therapy that blocks tissue inflammation, immune system response, and proliferation of activated joint fibroblasts (a type of cell believed to exacerbate the production of granulomas in tissue) may be the best way to fight rheumatoid arthritis.

Osteoporosis. It is thought that as much as 85% of the variance in individuals' bone mass is genetically determined. Stuart Ralston, a professor of medicine and bone metabolism at the University of Aberdeen in Scotland, believes osteoporosis also has many environmental factors, including diet, immobility, smoking, use of corticosteroids, coexisting disease, early menopause, and falling. (Alcohol consumption, on the other hand, appears to have a positive effect on bone mass). According to the National Osteoporosis Foundation, based in Washington, DC, osteoporosis is to blame for over 1.5 million fractures in the United States each year, a figure that includes some 300,000 hip fractures and approximately 700,000 vertebral fractures.

In a study published in the 9 April 1998 issue of the *New England Journal of Medicine*, Ralston and colleagues studied the occurrence of the SS, Ss, and ss genotypes (or combinations of alleles) of *COL1A1*, which is the gene for the bone-matrix protein collagen type I(alpha)1, among 1,778 postmenopausal women, divided into five-year age categories. They found that women who carried at least one copy of the s allele were more likely to be predisposed to osteoporotic fractures. Among the women aged 75–80, those with the ss genotype had a bone mineral density that was 12% lower at the femoral neck (the top of the thigh bone) and 20% lower at the lumbar spine (low back) than those women with the SS genotype. For women with the



Not just in the genes. New information shows that conditions such as obesity, arthritis, and osteoporosis are likely the result of a combination of genetic and environmental factors.

their natural habitat in the digestive tract and get into the lymph system, where they incite the development of granulomatous tissue. Rheumatoid arthritis patients routinely show immune responses against protein components of these bacteria even though no infection is apparent in the body.

SS genotype, bone mineral density at these sites was 5% and 3% lower, respectively, as compared to women with the *SS* genotype. But there's more to the story than just bone density.

According to Ralston, the increase in risk of fracture appears to be related to abnormal composition of the bone. Normal collagen in bone tissue is composed of two alpha 1 chains and one alpha 2 chain. Ralston's data suggest that the *s* allele may cause too many of the alpha 1 chains to be produced, resulting in bone tissue with a lower-than-normal percentage of alpha 2 chains. This makes the tissue unable to cross-link, or mesh, properly, depriving the bone of its usual tensile strength. The bone might therefore look normal and even have a normal density, but could still be structurally weak and vulnerable to fracture.

The symposium was rounded out with presentations on the role of gene-environment interactions in Alzheimer disease, diabetes, and asthma. Coordinator Perry Blackshear, director of clinical research at the NIEHS, said, "We're looking at nurture on top of nature leading to some of these clinical conditions."

Executive Order on Exotic Species

The United States is being invaded by aliens—alien plant, animal, and microbial species, that is. Nonindigenous species, also called exotics, are spreading through the United States, competing with native plants and preying on indigenous animals.

On 3 February 1999, President Bill Clinton signed an executive order to combat this threat, calling for the establishment of a national management plan for invasive species.

Nonindigenous species of weeds, insects, microbes, fish, and invertebrates steal into the United States in innumerable ways: weeds arrive at ports in farming equipment as seeds hidden in soil; aquatic invaders enter estuaries through ship

ballast water; insects, including disease-carrying mosquitoes, slip across national borders in nursery products and on timber and agricultural produce; and microbes can be carried by human travelers. In recent years, international trade and travel have been implicated worldwide in numerous epidemics of infectious diseases including rabies, tuberculosis, dengue, and cholera. In the United States, the nonindigenous diseases with the greatest public health impact are acquired immunodeficiency syndrome (AIDS) and influenza.

Alien species cost the United States \$123 billion a year, according to a 1999 study by Cornell University ecologist David Pimentel and colleagues. Nonindigenous species cause extensive damage to crops, rangeland, wetlands, and aquatic ecosystems.

For example, the green crab, a native of the European North Atlantic coast, arrived in North America in the early 19th century and established itself along the eastern seaboard from New Jersey to Nova Scotia. Since the late 1980s, though, the green crab has spread to

California. Wherever the crab ensconces itself, it eats voraciously, sharply reducing populations of commercially valuable clams and oysters, snails, and other crabs, with an estimated economic impact of \$44 million annually. European purple loosestrife, a weed introduced into the United States in the early 19th century as an ornamental, has spread to 48 states, infesting vast wetland acreage and costing \$45 million a year to fight.

Exotics can pose a serious threat to biodiversity, as well. About 400 of the 958 species on the United States' list of threatened or endangered species are at risk, mostly because of competition or predation by alien species.



Alien attack. Invasive species such as this green crab, shown attacking a cockle, can wreak havoc on sensitive native ecosystems by competing for food and living spaces.

Such invasions "are spinning out of control," says Phyllis Windle, who was project director of a comprehensive 1993 U.S. Environmental Protection Agency Office of Technology Assessment report, *Harmful Non-Indigenous Species in the United States*, and who is now a consultant on nonindigenous species issues. One problem in combating the threat is that responsibility for alien species has been scattered among 22 federal agencies, dozens of state agencies, and several thousand local agencies, Windle notes.

Federal agencies, including the U.S. Fish and Wildlife Service and the Department of Agriculture, have the most responsibility for preventing exotics from entering the country. But once an alien species has established itself and become a nuisance, it falls on understaffed state and local agencies to fight the threat, says Daniel Simberloff, a professor of environmental studies at the University of Tennessee at Knoxville.

Yet state and local officials often fail to compare notes on how they are battling such species. "Many places have similar problems with a species," says Windle, "but people on the ground in various states are not sharing information. There is no excuse, with the Internet available, not to coordinate responses."

Don C. Schmitz, a biologist at the Florida Department of Environmental Protection, says that a lack of communication among states means that "we often miss the window of opportunity to prevent an invader from spreading across state lines." Moreover, there are many species that are native to one part of the United States but alien to another, and states generally lack mechanisms to

